



Clinical trial results:

A Phase II Randomized, Double-Blind, Placebo-Controlled, Multicenter Study of VS 6063 in Subjects with Malignant Pleural Mesothelioma

Summary

EudraCT number	2013-001033-40
Trial protocol	GB BE ES SE NL NO PL IT
Global end of trial date	04 December 2015

Results information

Result version number	v1 (current)
This version publication date	30 December 2016
First version publication date	30 December 2016

Trial information

Trial identification

Sponsor protocol code	VS-6063-202
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01870609
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Verastem Inc
Sponsor organisation address	117 Kendrick Street, Suite 500, Needham, MA, United States, MA 02494
Public contact	Mahesh Padval, Verastem Inc, 001 7812924217, info@verastem.com
Scientific contact	Mahesh Padval, Verastem Inc, 001 7812924217, info@verastem.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	27 July 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	04 December 2015
Global end of trial reached?	Yes
Global end of trial date	04 December 2015
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objectives of the trial were to compare the overall survival (OS) in subjects with malignant pleural mesothelioma (MPM) receiving defactinib or placebo, and to compare the progression free survival (PFS) in these subjects.

Protection of trial subjects:

The study was performed in accordance with the protocol and the European Community CPMP guidelines of GCP for Trials on Medicinal Products and applicable regulatory requirements and in accordance with regulations and statutory instruments for the administration of radioactive substances. The study was in keeping with the requirements of the "Declaration of Helsinki" as adopted by the World Medical Association (WMA) General Assembly and with its subsequent amendments.

An independent data and safety monitoring committee was established to oversee the study to ensure patients' safety in this placebo-controlled trial.

Background therapy:

No background therapy was specified.

Prophylactic medications were permitted for use as needed if nausea was found to occur with administration of study drug and could not be managed with small amounts of food.

Evidence for comparator:

This was a placebo-controlled study. No active comparator was planned.

Actual start date of recruitment	25 September 2013
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Netherlands: 43
Country: Number of subjects enrolled	Norway: 2
Country: Number of subjects enrolled	Spain: 17
Country: Number of subjects enrolled	Sweden: 12
Country: Number of subjects enrolled	United Kingdom: 138
Country: Number of subjects enrolled	Belgium: 8
Country: Number of subjects enrolled	Italy: 2
Country: Number of subjects enrolled	France: 17
Country: Number of subjects enrolled	Australia: 20
Country: Number of subjects enrolled	South Africa: 1
Country: Number of subjects enrolled	United States: 31
Country: Number of subjects enrolled	Japan: 42

Country: Number of subjects enrolled	New Zealand: 11
Worldwide total number of subjects	344
EEA total number of subjects	239

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	110
From 65 to 84 years	231
85 years and over	3

Subject disposition

Recruitment

Recruitment details:

449 subjects were screened and 344 were randomised and treated in 72 centres worldwide between 25 Sep 2013 and 04 Dec 2015, including 42 in the EU.

Pre-assignment

Screening details:

Male and female subjects aged at least 18 years, with histologically-proven MPM, evaluable disease according to RECIST v1.1, with ongoing confirmed partial or complete response to one previous chemotherapy regimen (at least 4 cycles), with last dose of chemotherapy administered at most 6 weeks previously, and a life expectancy of at least 3 months.

Period 1

Period 1 title	Baseline
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Assessor

Blinding implementation details:

Defactinib was formulated as a white to off-white oval tablet for oral administration and supplied in single unit dose strength of 200 mg. A matched placebo control was also provided. The placebo was the same color, shape, and composition, but contained no active ingredients.

Arms

Are arms mutually exclusive?	Yes
Arm title	Defactinib

Arm description:

Defactinib was taken orally twice daily in continuous 21 day cycles. The dose of defactinib was 400 mg (2 × 200 mg) twice daily.

Arm type	Experimental
Investigational medicinal product name	Defactinib
Investigational medicinal product code	VS-6063
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Defactinib was taken orally twice daily in continuous 21 day cycles. The dose of defactinib was 400 mg (2 × 200 mg) twice daily.

Arm title	Placebo
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Arm description:

Placebo was taken orally twice daily in continuous 21 day cycles.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Placebo was taken orally twice daily in continuous 21 day cycles.

Number of subjects in period 1	Defactinib	Placebo
Started	173	171
Completed	173	171

Period 2

Period 2 title	Treatment period
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst
Blinding implementation details: As described for baseline period	

Arms

Are arms mutually exclusive?	Yes
Arm title	Defactinib
Arm description: As defined for baseline period	
Arm type	Experimental
Investigational medicinal product name	Defactinib
Investigational medicinal product code	VS-6063
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: 400 mg twice daily	
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: Twice daily	
Arm title	Placebo
Arm description: As defined for baseline period	
Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:
2 x 200mg tablet taken twice daily

Number of subjects in period 2	Defactinib	Placebo
Started	173	171
Completed	0	0
Not completed	173	171
Adverse event, serious fatal	55	58
Termination of study	112	109
Unknown	6	4

Baseline characteristics

Reporting groups

Reporting group title	Defactinib
Reporting group description:	
Defactinib was taken orally twice daily in continuous 21 day cycles. The dose of defactinib was 400 mg (2 × 200 mg) twice daily.	
Reporting group title	Placebo
Reporting group description:	
Placebo was taken orally twice daily in continuous 21 day cycles.	

Reporting group values	Defactinib	Placebo	Total
Number of subjects	173	171	344
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	56	54	110
From 65-84 years	114	117	231
85 years and over	3	0	3
Age continuous			
Data reported at enrolment			
Units: years			
arithmetic mean	67.7	67.6	
standard deviation	± 8.33	± 8.67	-
Gender categorical			
Units: Subjects			
Female	28	28	56
Male	145	143	288
Karnofsky performance score			
Baseline Karnofsky performance score			
Units: Subjects			
70	6	6	12
80	49	48	97
90	82	84	166
100	36	33	69
Race			
Race of randomised subjects			
Units: Subjects			
White	149	149	298
Black	1	1	2
Asian	22	20	42
Other	1	1	2
Primary disease location			

The location of primary tumour			
Units: Subjects			
Ipsilateral	26	14	40
Parietal pleura	91	90	181
Visceral pleura	9	24	33
Lung parenchyma	4	2	6
Mediastinal	12	9	21
Other	31	29	60
Unknown	0	3	3
Metastasis location			
Location of metastatic tumours for subjects with metastases			
Units: Subjects			
Lung	6	10	16
Mediastinum	2	3	5
Liver	3	2	5
Adrenal	1	1	2
Bone	0	3	3
Other	31	25	56
None	130	127	257
TNM stage			
TNM classification of malignant tumours			
Units: Subjects			
Stage I	2	2	4
Stage IA	4	8	12
Stage IB	11	10	21
Stage II	27	31	58
Stage III	66	58	124
Stage IV	47	49	96
Unknown	16	13	29
Body mass index			
Data reported at baseline			
Units: kg/m2			
arithmetic mean	25.63	26.2	
standard deviation	± 3.838	± 4.592	-
Time since diagnosis			
Time since original histopathological diagnosis of MPM			
Units: Months			
arithmetic mean	6.1	6.7	
standard deviation	± 5.4	± 5.66	-
Overall quality of life score			
Lung cancer Symptom scale modified for mesothelioma			
Units: Score			
median	79.31	77.63	
full range (min-max)	9 to 100	31 to 100	-
Quality of life - pain			
Lung cancer Symptom scale modified for mesothelioma			
Units: Score			
median	92.5	92	
full range (min-max)	1 to 100	15 to 100	-
Quality of life - dyspnoea			
Lung cancer Symptom scale modified for mesothelioma			

Units: Score			
median	81.5	77	
full range (min-max)	7 to 100	6 to 100	-

End points

End points reporting groups

Reporting group title	Defactinib
Reporting group description: Defactinib was taken orally twice daily in continuous 21 day cycles. The dose of defactinib was 400 mg (2 × 200 mg) twice daily.	
Reporting group title	Placebo
Reporting group description: Placebo was taken orally twice daily in continuous 21 day cycles.	
Reporting group title	Defactinib
Reporting group description: As defined for baseline period	
Reporting group title	Placebo
Reporting group description: As defined for baseline period	

Primary: Progression free survival

End point title	Progression free survival
End point description: Time to disease progression or death	
End point type	Primary
End point timeframe: From baseline to termination of the study	

End point values	Defactinib	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	173	171		
Units: Months				
median (confidence interval 95%)	4.11 (2.79 to 5.55)	4.04 (2.79 to 4.17)		

Statistical analyses

Statistical analysis title	Duration of PFS
Statistical analysis description: The primary analysis of PFS was based on the stratified log-rank test, and used Kaplan-Meier methods for estimation of summary statistics. The median duration of PFS was estimated based on the 50th percentile of the Kaplan-Meier distribution. If applicable, p-values for the log-rank test were computed.	
Comparison groups	Defactinib v Placebo

Number of subjects included in analysis	344
Analysis specification	Pre-specified
Analysis type	superiority ^[1]
Parameter estimate	Hazard ratio (HR)
Point estimate	0.967
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.711
upper limit	1.316

Notes:

[1] - The primary analysis of PFS was based on the stratified log-rank test, and used Kaplan-Meier methods for estimation of summary statistics. Hazard ratio with respect to relapse or death and 95% CI was calculated using Cox's proportional hazard model, stratified by Merlin status.

Secondary: Overall survival

End point title	Overall survival
End point description:	
Duration of overall survival; subjects still alive at the time point of analysis or who dropped out prior to study end were censored at the day they were last known to be alive.	
End point type	Secondary
End point timeframe:	
Baseline to termination of the study	

End point values	Defactinib	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	173	171		
Units: Months				
median (confidence interval 95%)	12.68 (9.33 to 20.99)	13.57 (9.49 to 21.16)		

Statistical analyses

No statistical analyses for this end point

Secondary: Objective response rate

End point title	Objective response rate
End point description:	
Response to study drug according to RECIST v1.1 where objective response rate included subjects with complete or partial responses. Best objective response was categorised as complete response, partial response, stable disease, or progressive disease.	
End point type	Secondary
End point timeframe:	
From baseline to termination of the study	

End point values	Defactinib	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	173	171		
Units: Subjects				
Complete/partial response	7	5		
Complete response	0	0		
Partial response	7	5		
Stable disease	101	104		
Progressive disease	46	50		

Statistical analyses

Statistical analysis title	Difference in best objective response rate
Statistical analysis description:	
Frequencies and proportions of best objective responses were presented overall. Proportions of subjects with results of complete response, PR, SD, and PD were to be compared between the treatment arms, accounting for randomization strata using a Cochran Mantel-Haenszel chi-square test.	
Comparison groups	Defactinib v Placebo
Number of subjects included in analysis	344
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5093
Method	Cochran-Mantel-Haenszel

Secondary: Overall quality of life score

End point title	Overall quality of life score
End point description:	
Lung cancer Symptom scale modified for mesothelioma	
End point type	Secondary
End point timeframe:	
End of treatment	

End point values	Defactinib	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	123	112		
Units: score				
median (full range (min-max))	70.88 (16 to 100)	76.06 (18 to 100)		

Statistical analyses

No statistical analyses for this end point

Secondary: Quality of life - pain

End point title	Quality of life - pain
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End point description:

Lung cancer Symptom scale modified for mesothelioma

End point type	Secondary
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End point timeframe:

End of treatment

End point values	Defactinib	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	123	112		
Units: Score				
median (full range (min-max))	81 (12 to 100)	84 (6 to 100)		

Statistical analyses

No statistical analyses for this end point

Secondary: Quality of life - dyspnoea

End point title	Quality of life - dyspnoea
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End point description:

Lung cancer Symptom scale modified for mesothelioma

End point type	Secondary
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End point timeframe:

End of treatment

End point values	Defactinib	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	123	112		
Units: Score				
median (full range (min-max))	70 (3 to 100)	73.5 (13 to 100)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the time that the subject provided informed consent through and including 30 calendar days after the last administration of study drug

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	16.0
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Reporting groups

Reporting group title	Defactinib
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Reporting group description:

Defactinib was taken orally twice daily in continuous 21 day cycles. The dose of defactinib was 400 mg (2 × 200 mg) twice daily.

Reporting group title	Placebo
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Reporting group description:

Placebo was taken orally twice daily in continuous 21 day cycles.

Serious adverse events	Defactinib	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	19 / 173 (10.98%)	13 / 171 (7.60%)	
number of deaths (all causes)	6	1	
number of deaths resulting from adverse events	1	1	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant neoplasm progression			
subjects affected / exposed	4 / 173 (2.31%)	1 / 171 (0.58%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 4	0 / 1	
Cancer pain			
subjects affected / exposed	0 / 173 (0.00%)	1 / 171 (0.58%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to spine			
subjects affected / exposed	1 / 173 (0.58%)	0 / 171 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericarditis malignant			

subjects affected / exposed	0 / 173 (0.00%)	1 / 171 (0.58%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Plasma cell myeloma			
subjects affected / exposed	1 / 173 (0.58%)	0 / 171 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Electrocardiogram QT prolonged			
subjects affected / exposed	1 / 173 (0.58%)	0 / 171 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Jugular vein thrombosis			
subjects affected / exposed	1 / 173 (0.58%)	0 / 171 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vena cava thrombosis			
subjects affected / exposed	0 / 173 (0.00%)	1 / 171 (0.58%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 173 (0.00%)	2 / 171 (1.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure congestive			
subjects affected / exposed	1 / 173 (0.58%)	0 / 171 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericardial effusion			
subjects affected / exposed	1 / 173 (0.58%)	0 / 171 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Syncope			
subjects affected / exposed	1 / 173 (0.58%)	0 / 171 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Neuralgia			
subjects affected / exposed	0 / 173 (0.00%)	1 / 171 (0.58%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 173 (0.58%)	0 / 171 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza like illness			
subjects affected / exposed	0 / 173 (0.00%)	1 / 171 (0.58%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	1 / 173 (0.58%)	1 / 171 (0.58%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal distension			
subjects affected / exposed	1 / 173 (0.58%)	0 / 171 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain			
subjects affected / exposed	1 / 173 (0.58%)	0 / 171 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain upper			

subjects affected / exposed	1 / 173 (0.58%)	0 / 171 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	0 / 173 (0.00%)	1 / 171 (0.58%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intussusception			
subjects affected / exposed	1 / 173 (0.58%)	0 / 171 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	0 / 173 (0.00%)	1 / 171 (0.58%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 173 (0.58%)	0 / 171 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	1 / 173 (0.58%)	0 / 171 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemoptysis			
subjects affected / exposed	1 / 173 (0.58%)	0 / 171 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	0 / 173 (0.00%)	1 / 171 (0.58%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			

Renal failure			
subjects affected / exposed	1 / 173 (0.58%)	0 / 171 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 173 (0.58%)	0 / 171 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal chest pain			
subjects affected / exposed	1 / 173 (0.58%)	0 / 171 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Pneumonia			
subjects affected / exposed	1 / 173 (0.58%)	0 / 171 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Lung infection			
subjects affected / exposed	1 / 173 (0.58%)	1 / 171 (0.58%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchopneumonia			
subjects affected / exposed	1 / 173 (0.58%)	0 / 171 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Empyema			
subjects affected / exposed	0 / 173 (0.00%)	1 / 171 (0.58%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection			
subjects affected / exposed	0 / 173 (0.00%)	1 / 171 (0.58%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Upper respiratory tract infection subjects affected / exposed	1 / 173 (0.58%)	0 / 171 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hyperkalaemia			
subjects affected / exposed	0 / 173 (0.00%)	1 / 171 (0.58%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Defactinib	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	161 / 173 (93.06%)	139 / 171 (81.29%)	
Investigations			
Blood creatinine decreased			
subjects affected / exposed	12 / 173 (6.94%)	6 / 171 (3.51%)	
occurrences (all)	12	6	
Blood bilirubin increased			
subjects affected / exposed	15 / 173 (8.67%)	1 / 171 (0.58%)	
occurrences (all)	15	1	
Nervous system disorders			
Dizziness			
subjects affected / exposed	12 / 173 (6.94%)	4 / 171 (2.34%)	
occurrences (all)	12	4	
Paraesthesia			
subjects affected / exposed	9 / 173 (5.20%)	3 / 171 (1.75%)	
occurrences (all)	9	3	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	30 / 173 (17.34%)	27 / 171 (15.79%)	
occurrences (all)	30	27	
Oedema peripheral			
subjects affected / exposed	22 / 173 (12.72%)	13 / 171 (7.60%)	
occurrences (all)	22	13	

Non-cardiac chest pain subjects affected / exposed occurrences (all)	11 / 173 (6.36%) 11	14 / 171 (8.19%) 14	
Chest pain subjects affected / exposed occurrences (all)	11 / 173 (6.36%) 11	13 / 171 (7.60%) 13	
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	9 / 173 (5.20%) 9	3 / 171 (1.75%) 3	
Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all)	42 / 173 (24.28%) 42	19 / 171 (11.11%) 19	
Diarrhoea subjects affected / exposed occurrences (all)	41 / 173 (23.70%) 41	15 / 171 (8.77%) 15	
Constipation subjects affected / exposed occurrences (all)	21 / 173 (12.14%) 21	16 / 171 (9.36%) 16	
Vomiting subjects affected / exposed occurrences (all)	19 / 173 (10.98%) 19	11 / 171 (6.43%) 11	
Respiratory, thoracic and mediastinal disorders Dyspnoea subjects affected / exposed occurrences (all)	30 / 173 (17.34%) 30	24 / 171 (14.04%) 24	
Cough subjects affected / exposed occurrences (all)	24 / 173 (13.87%) 24	17 / 171 (9.94%) 17	
Lower respiratory tract infection subjects affected / exposed occurrences (all)	7 / 173 (4.05%) 7	11 / 171 (6.43%) 11	
Hepatobiliary disorders Hyperbilirubinaemia			

subjects affected / exposed occurrences (all)	14 / 173 (8.09%) 14	0 / 171 (0.00%) 0	
Skin and subcutaneous tissue disorders Rash subjects affected / exposed occurrences (all)	8 / 173 (4.62%) 8	8 / 171 (4.68%) 8	
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) Musculoskeletal pain subjects affected / exposed occurrences (all) Back pain subjects affected / exposed occurrences (all)	20 / 173 (11.56%) 20 6 / 173 (3.47%) 6 10 / 173 (5.78%) 10	5 / 171 (2.92%) 5 12 / 171 (7.02%) 12 4 / 171 (2.34%) 4	
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all)	11 / 173 (6.36%) 11	4 / 171 (2.34%) 4	
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	31 / 173 (17.92%) 31	13 / 171 (7.60%) 13	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported